## REMARKS

This document is filed in response to the final office action dated September 17, 2003 ("Office Action"). Applicant has amended claim 1 to promote clarity, to correct a typographical error, and to limit the recited S-layer protein fragments to the C-terminal 120 - 405 residues of the protein. **The amendments should be entered as they raise no new issues that will require further consideration or search and also do not touch the merits of the application within the meaning of 37 C.F.R. § 1.116(b).**

Note that support for the amendments appears throughout the specification and in the claims originally filed. In particular, support for "insoluble fusion protein," can be found at page 6, lines 19-23. Support for "first component remains insoluble" can be found at page 7, lines 3-4 and 29-30. Support for "a C. crescentus S-layer protein fragment of at least about 120 amino acids of the C-terminal and no more than about 405 amino acids of the C-terminal" can be found at page 9, lines 19-23 and the amino acid sequence disclosed at pages 21-23.[1] No new matter has been introduced.

Claims 1-8 are pending. Among them, claims 7-8 have been withdrawn from further consideration as being drawn to non-elected inventions. Claims 1-6 are now under examination. Reconsideration of this application is requested in view of the following remarks:

### Claim objection

Claim 1 was objected to for containing a typographical error. See the Office Action, page 2, lines 16-17. Applicant has corrected this error.

### Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-6 under § 112, first paragraph on two different grounds.

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[1] These parts of the specification teach C-terminal fragments of C. crescentus S-layer protein having respectively amino acid residues 622, 690, 784, 892, and 907 to amino acid residue 1026. The minimal and maximal lengths of the fragments are 120 (120=1026-907+1) and 405 (405=1026-622+1), respectively. In other words, the specification provides support for "a C. crescentus S-layer protein fragment of at least about 120 amino acids of the C-terminal and no more than about 405 amino acids of the C-terminal."

Applicant will address each of the grounds below:

I

Claims 1-6 were rejected for containing subject matter not described in the specification. More specifically, the Examiner asserted that the specification did not provide support for the phrase "a Caulobacter crescentus S-layer protein fragment incapable of adhesion to a Caulobacter crescentus cell surface" recited in rejected claim 1. See the Office Action, the paragraph bridging pages 2 and 3. Applicant submits that the ground for rejection has been overcome by the amendments set forth above and requests that the rejection be withdrawn.

II

The Examiner also rejected claims 1-6 for lack of enablement. See the Office Action, pages 3-5, part 8. According to the Examiner, "the claims broadly encompass any Caulobacter crescentus S-layer protein fragments" and "an undue amount of experimentation would be required to determine those fragments ... that can be used to practice the claimed invention." See page 4, lines 17-18 and page 5, lines 9-10, respectively.

Applicant has amended claim 1 to limit the S-layer protein fragments to the C-terminal 120 - 405 residues and provided working examples of such fragments in the specification. See, e.g., Examples 1-4 on pages 15-18. Also, the art provides adequate guidance as to how to select a fragment of the Caulobacter crescentus S-layer protein that can be used to practice the claimed method. See, e.g., Smit et al., column 5, line 56 through column 8, line 34.

Thus, in view of the above remarks, Applicant submits that claim 1 is enabled. By the same token, claims 2-6 are also enabled.

Rejection under 35 U.S.C. § 103(a)

Claims 1-6 were rejected as being obvious over Smit et al. in view of Nomellini et al. (J. Bactriol. 179: 6349-6354), Ausubel et al. (Current Protocols in Molecular Biology, John Wiley and Sons, Inc., 1994), and Better (U.S. Patent No. 5,851,802). See the Office Action, Part 9, pages 5-9,.

As described above, amended claim 1 is drawn to a method of cleaving an insoluble fusion protein containing a fragment of the Caulobacter crescentus S-layer protein and a

component heterologous to Caulobacter. The method involves treating the fusion protein with an acidic solution such that an Asp-Pro bond in the fusion protein is cleaved and the fragment of the Caulobacter crescentus S-layer protein remains **insoluble** after cleavage.

According to the Examiner, (1) Smit et al., teaches expression and secretion of heterologous polypeptides from Caulobacter; (2) Ausubel et al. teaches hydrolysis of an Asp-Pro bond in a fusion protein at low pH; and (3) Better discloses cleavage of an Asp-Pro bound in an insoluble Bone D-BPI peptide fusion protein at acidic pH, resulting in insoluble Bone D and soluble BPI peptide. As pointed out in Applicant's response dated July 10, 2003, neither of these three references, alone or combined, suggests that a Caulobacter crescentus S-layer protein fragment would remain insoluble after cleavage at low pH, as required in claim 1. It is the Examiner's position that Nomellini et al. ("Nomellini") provides the missing link by teaching that full-length Caulobacter crescentus S-layer protein is "resistant to acid solubilization." See the Office Action, page 6, lines 20-21. As such, the four references would have suggested the method of claim 1.

However, Applicant would like to point out that "resistant to ... solubilization" is not equivalent to "insoluble." In fact, Nomellini teaches that full-length S-layer protein is generally **soluble** at low pH. See page 6351, right column, lines 6-35. Also, Nomellini does not suggest any S-layer protein fragment, such as those recited in amended claim 1, that is insoluble at low pH. Accordingly, contrary to the Examiner's position, this reference does not provide the missing link above. Indeed, in view of this reference's teaching that full-length S-layer protein is generally **soluble** at low pH, it **teaches away** from using an S-layer protein or its fragment as a fusion protein carrier. Thus, the four references do not render obvious the method of claim 1. Neither do they render obvious claims 2-6, all of which depend from claim 1.

## CONCLUSION

Applicant submits that the grounds for objection and rejection asserted by the Examiner have been overcome, and the claims, as pending, define subject matter that is enabled and nonobvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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